

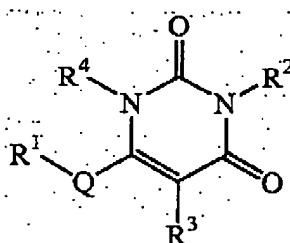
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AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of claims:**1 (currently amended).** A compound of Formula I

I

or a pharmaceutically acceptable salt thereof,

wherein:

 R^1 is independently selected from:

- C_3 -or C_6 -cycloalkyl (C_4 - C_8 -alkylenyl)_m;
- Substituted C_5 -or C_6 -cycloalkyl (C_4 - C_8 -alkylenyl)_m;
- C_8 - C_{10} -bicycloalkyl (C_4 - C_8 -alkylenyl)_m;
- Substituted C_8 - C_{10} -bicycloalkyl (C_4 - C_8 -alkylenyl)_m;
- ~~5- or 6 membered heterocycloalkyl (C_4 - C_8 -alkylenyl)_m;~~
- Substituted ~~5- or 6 membered heterocycloalkyl (C_4 - C_8 -alkylenyl)_m;~~
- ~~8- to 10 membered heterobicycloalkyl (C_4 - C_8 -alkylenyl)_m;~~
- Substituted ~~8- to 10 membered heterobicycloalkyl (C_4 - C_8 -alkylenyl)_m;~~
- Phenyl (C_4 - C_8 -alkylenyl)_m;
- Substituted phenyl (C_4 - C_8 -alkylenyl)_m;
- Naphthyl (C_4 - C_8 -alkylenyl)_m;
- Substituted naphthyl (C_4 - C_8 -alkylenyl)_m;
- ~~5- or 6 membered heteroaryl (C_4 - C_8 -alkylenyl)_m;~~
- Substituted ~~5- or 6 membered heteroaryl (C_4 - C_8 -alkylenyl)_m;~~

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~~8 to 10 membered heterobiaryl (C₁-C₈ alkylene)~~_m;

~~Substituted 8 to 10 membered heterobiaryl (C₁-C₈ alkylene)~~_m;

~~5 or 6 membered heterocycloalkyl-phenylene~~ (C₁-C₈ alkylene)_m;

~~Substituted 5 or 6 membered heterocycloalkyl-phenylene~~ (C₁-C₈ alkylene)_m;

~~Biphenyl (C₁-C₈ alkylene)~~_m;

~~Substituted biphenyl (C₁-C₈ alkylene)~~_m;

~~5 or 6 membered heteroaryl-phenylene~~ (C₁-C₈ alkylene)_m;

~~Substituted 5 or 6 membered heteroaryl-phenylene~~ (C₁-C₈ alkylene)_m;

~~5 or 6 membered heteroaryl (5 or 6 membered heteroarylenyl) (C₁-C₈ alkylene)~~_m;

~~Substituted 5 or 6 membered heteroaryl (5 or 6 membered heteroarylenyl) (C₁-C₈ alkylene)~~_m;

~~Phenyl L (5 or 6 membered heteroarylenyl) (C₁-C₈ alkylene)~~_m;

~~Substituted phenyl L (5 or 6 membered heteroarylenyl) (C₁-C₈ alkylene)~~_m;

~~8 to 10 membered heterobiaryl-phenylene~~ (C₁-C₈ alkylene)_m;

~~Substituted 8 to 10 membered heterobiaryl-phenylene~~ (C₁-C₈ alkylene)_m;

~~Phenyl (5 or 6 membered heteroarylenyl) (C₁-C₈ alkylene)~~_m;

~~Substituted phenyl (5 or 6 membered heteroarylenyl) (C₁-C₈ alkylene)~~_m;

~~Naphthyl (5 or 6 membered heteroarylenyl) (C₁-C₈ alkylene)~~_m;

~~Substituted naphthyl (5 or 6 membered heteroarylenyl) (C₁-C₈ alkylene)~~_m;

~~Phenyl (8 to 10 membered heterobiarylenyl) (C₁-C₈ alkylene)~~_m and

~~Substituted phenyl (8 to 10 membered heterobiarylenyl) (C₁-C₈ alkylene)~~_m;

~~R² is independently selected from:~~

~~H;~~

~~C₁-C₆ alkyl;~~

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Phenyl-(C₁-C₈ alkylene)_m;

Substituted phenyl-(C₁-C₈ alkylene)_m;

Naphthyl-(C₁-C₈ alkylene)_m;

Substituted naphthyl-(C₁-C₈ alkylene)_m;

5- or 6-membered heteroaryl-(C₁-C₈ alkylene)_m;

Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylene)_m;

8- to 10-membered heterobiaryl-(C₁-C₈ alkylene)_m;

Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylene)_m;

Phenyl-O-(C₁-C₈ alkylene);

Substituted phenyl-O-(C₁-C₈ alkylene);

Phenyl-S-(C₁-C₈ alkylene);

Substituted phenyl-S-(C₁-C₈ alkylene);

Phenyl-S(O)-(C₁-C₈ alkylene);

Substituted phenyl-S(O)-(C₁-C₈ alkylene);

Phenyl-S(O)₂-(C₁-C₈ alkylene); and

Substituted phenyl-S(O)₂-(C₁-C₈ alkylene);

R¹ is independently selected from:

Phenyl-(C₁-C₈ alkylene);

Substituted phenyl-(C₁-C₈ alkylene);

5- or 6-membered heteroaryl-(C₁-C₈ alkylene);

Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylene);

8- to 10-membered heterobiaryl-(C₁-C₈ alkylene); and

Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylene); and

R² is independently selected from:

Phenyl-(C₁-C₈ alkylene)_m;

Substituted phenyl-(C₁-C₈ alkylene)_m;

5- or 6-membered heteroaryl-(C₁-C₈ alkylene)_m;

Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylene)_m;

8- to 10-membered heterobiaryl-(C₁-C₈ alkylene)_m; and

Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylene)_m;

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Each substituted R¹ and R² group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C₁-C₆ alkyl;
CN;
CF₃;
HO;
(C₁-C₆ alkyl)-O;
(C₁-C₆ alkyl)-S;
(C₁-C₆ alkyl)-S(O);
(C₁-C₆ alkyl)-S(O)₂;
O₂N;
H₂N;
(C₁-C₆ alkyl)-N(H);
(C₁-C₆ alkyl)₂-N;
(C₁-C₆ alkyl)-C(O)O-(C₁-C₈ alkylene);
(C₁-C₆ alkyl)-C(O)O-(1- to 8-membered heteroalkylene);
(C₁-C₆ alkyl)-C(O)N(H)-(C₁-C₈ alkylene);
(C₁-C₆ alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylene);
H₂NS(O)₂-(C₁-C₈ alkylene);
(C₁-C₆ alkyl)-N(H)S(O)₂-(C₁-C₈ alkylene);
(C₁-C₆ alkyl)₂-NS(O)₂-(C₁-C₈ alkylene);
3- to 6-membered heterocycloalkyl-(G)_m;
Substituted 3- to 6-membered heterocycloalkyl-(G)_m;
5- or 6-membered heteroaryl-(G)_m;
Substituted 5- or 6-membered heteroaryl-(G)_m;
(C₁-C₆ alkyl)-S(O)₂-N(H)-C(O)-(C₁-C₈ alkylene); and
(C₁-C₆ alkyl)-C(O)-N(H)-S(O)₂-(C₁-C₈ alkylene);

wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

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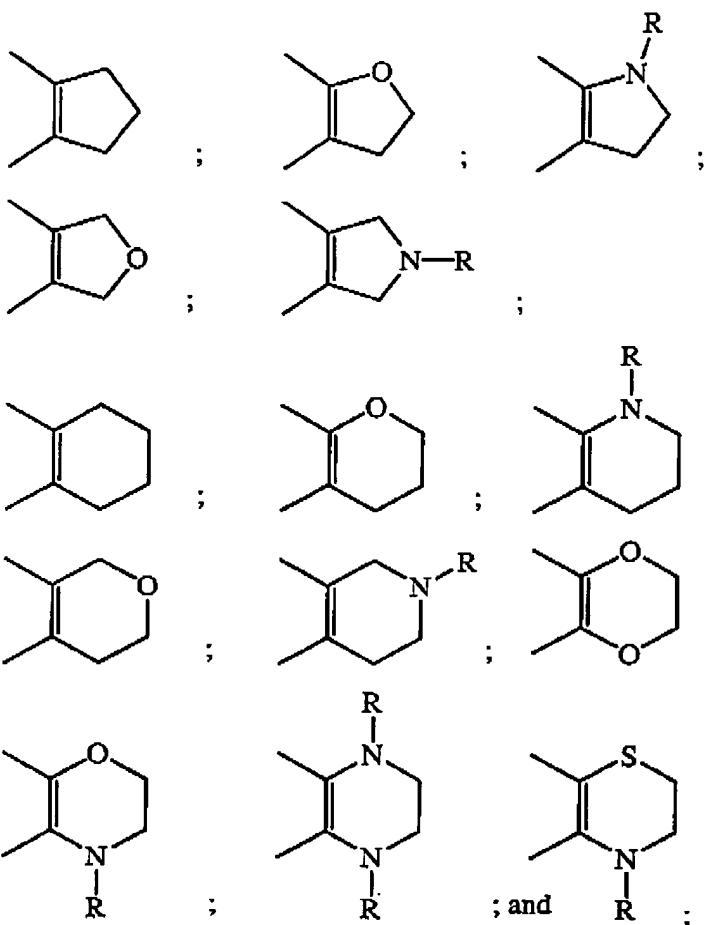
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 HO_2C ;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group $\text{C}=\text{O}$;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



R is H or $\text{C}_1\text{-C}_6$ alkyl;

G is CH_2 , O , S , $\text{S}(\text{O})$; or $\text{S}(\text{O})_2$;

Each m is independently selected from an integer of 0 or 1;

R^3 is independently selected from the groups:

H ;

CH_3 ;

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CH₃O;CH=CH₂;

HO;

CF₃;

CN;

HC(O);

CH₃C(O);

HC(NOH);

H₂N;(CH₃)-N(H);(CH₃)₂-N;H₂NC(O);(CH₃)-N(H)C(O);(CH₃)₂-NC(O);

Halo; and

CO₂H;Q is Q; independently selected from O, S, S(O), S(O)₂, and N(R⁵);L is independently selected from CH₂, C(O), O, S, S(O), S(O)₂, and N(R⁶);R⁴, R⁵, and R⁶ are independently H or C₁-C₆ alkyl;wherein each C₈-C₁₀ bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double

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bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C₁-C₆ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C₁-C₆ alkyl)₂-N group, the C₁-C₆ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

wherein each group and each substituent recited above is independently selected.

2 to 6 (canceled).

7 (currently amended). ~~The compound according to Claim 1, A compound selected from:~~

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3-Benzyl-6-[2-[3-(2,4-dichloro-phenyl)-isoxazol-5-yl]-2-oxo-ethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[5-(4-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[3-(4-methoxy-phenyl)-isoxazol-5-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[3-(2,6-dichloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[5-(2-chloro-phenyl)-isoxazol-3-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[2-(4-chloro-phenyl)-thiazol-4-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[5-(4-methoxy-phenyl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[3-(4-chloro-phenyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[3-(4-chloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

6-(4-Amino-5-phenyl-4H-[1,2,4]triazol-3-ylsulfanyl)-3-benzyl-5-methyl-1H-pyrimidine-2,4-dione;

or a pharmaceutically acceptable salt thereof.

8 (currently amended). The compound according to Claim 1, A compound selected from:

3-Benzyl-5-methyl-6-[5-(2-methylsulfanyl-pyridin-3-yl)-[1,2,4]oxadiazol-3-ylmethylsulfanyl]-1H-pyrimidine-2,4-dione;

3-Benzyl-5-methyl-6-(3-phenyl-isoxazol-5-ylmethylsulfanyl)-1H-pyrimidine-2,4-dione;

3-Benzyl-5-methyl-6-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-1H-pyrimidine-2,4-dione;

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3-Benzyl-5-methyl-6-(5-phenyl-[1,2,4]oxadiazol-3-ylmethylsulfanyl)-1H-pyrimidine-2,4-dione;

3-Benzyl-5-methyl-6-(2-phenyl-thiazol-4-ylmethylsulfanyl)-1H-pyrimidine-2,4-dione;

3-Benzyl-5-methyl-6-[3-(4-nitro-benzyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-1H-pyrimidine-2,4-dione;

3-Benzyl-6-[5-(4-chloro-phenylamino)-2H-[1,2,4]triazol-3-ylsulfanyl]-5-methyl-1H-pyrimidine-2,4-dione;

6-(Benzothiazol-2-ylsulfanyl)-3-benzyl-5-methyl-1H-pyrimidine-2,4-dione; and

3-Benzyl-6-(6-methoxy-benzothiazol-2-ylamino)-5-methyl-1H-pyrimidine-2,4-dione;

or a pharmaceutically acceptable salt thereof.

9 (currently amended). The compound according to Claim 1, A compound selected from:

3-Benzyl-6-[3-(2,6-dichloro-phenyl)-isoxazol-5-ylmethylsulfanyl]-1,5-dimethyl-1H-pyrimidine-2,4-dione;

3-Benzyl-1,5-dimethyl-6-[5-(3-methyl-4-nitro-phenyl)-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-1H-pyrimidine-2,4-dione;

3-Benzyl-1,5-dimethyl-6-[5-naphthalen-2-yl-[1,3,4]oxadiazol-2-ylmethylsulfanyl]-1H-pyrimidine-2,4-dione;

3-Benzyl-1,5-dimethyl-6-(5-phenyl-isoxazol-3-ylmethylsulfanyl)-1H-pyrimidine-2,4-dione; and

3-Benzyl-1,5-dimethyl-6-[3-(4-nitro-benzyl)-[1,2,4]oxadiazol-5-ylmethylsulfanyl]-1H-pyrimidine-2,4-dione;

or a pharmaceutically acceptable salt thereof.

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10 (original). A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

11 (currently amended). ~~The pharmaceutical composition according to Claim 10, A pharmaceutical composition,~~ comprising a compound according to any one of Claims 7 to 9, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

12 (original). A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

13 (currently amended). ~~The method according to Claim 12, wherein the compound administered is A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to any one of Claims 7 to 9, or a pharmaceutically acceptable salt thereof.~~